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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,386	12/27/2004	Marie-Noelle Horcajada	P70350US0	6940

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EXAMINER	
JAVANMARD, SAHAR	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
12/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,386	HORCAJADA ET AL.	
	Examiner	Art Unit	
	SAHAR JAVANMARD	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-11 and 13-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-11 and 13-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/28/2008 has been entered.

Claim(s) 4, 5, 7-9, 15, 16, 18, 19, and 21 have been amended. Claim(s) 2-11 and 13-22 are examined herein.

Applicant's amendments have rendered the 112 1st rejection of claims 4, 5, 7, 15, 16 and 18 of the last Office Action moot, therefore hereby withdrawn.

Applicant's arguments with respect to the 102(b) rejection of claims 2-9, 11, 12-20 and 22 as being anticipated by Wenzel et al. (EP 1127572A2) has been fully considered and are persuasive. The rejection is hereby withdrawn.

Applicant's arguments with respect to the 102(b) rejection of claims 2-7, 9-10, 13-19 and 21-22 as being anticipated by Kise et al (JP 2001114675A) have been fully considered but are not persuasive as Applicant is arguing based on amended claims. Since Applicant has amended the claims, said rejection is hereby withdrawn.

Applicant's arguments with respect to the 103(a) rejection of claim 9 as being unpatentable over Wenzel in view of Barnes et al. (US Patent No. 5,506,211) have been

fully considered but are not persuasive. A modified 103 rejection follows in the office action below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2-8, 10-11, and 13-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wenzel et al. (EP 1127572A2) of record as evidenced by (Katori, et

al., *Inflammatory Research*, 2000) of record and Hofbauer et al (*Journal of Molecular Medicine*, 2001) of record.

Wenzel teaches compositions of flavone-type compounds of formula II, specifically hesperidin (Table 3) are useful in the treatment of cyclooxygenase-2 (COX-2) and nuclear factor kappa B (NF-kβ) mediated diseases (page 2, lines 23-24).

Wenzel teaches the compositions of the compounds of formula II may be used as dietary supplements, added as the active ingredient to foods or medical foods or as oral compositions to treat COX-2 and NF-kβ mediated diseases (page 8, lines 33-37; page 11, example 1; page 12, examples 5 and 6).

The reference teaches the compounds of formula I can be added to nutritional substances which can be a food preparation or an essential nutrient preparation. Food preparations particularly well suited include breakfast foods, such as prepared cereals, toaster pastries, and breakfast drink mixes; infant formulas; dietary supplements; complete diet formulas; and weight-loss preparations, such as weight-loss drinks and weight-loss bars (page 10, lines 50-52; page 11, example 1; page 12, example 6).

Furthermore, in example 6, an infant formula containing the flavone is administered.

Wenzel teaches the daily quantity of compounds of formula I by oral administration is between 10 mg to 700 mg (page 11 and 12, examples).

Wenzel teaches the pharmaceutical compositions of formula I for the treatment of COX-2 and NF-kB mediated diseases to humans and other animals administered orally,

rectally, parenterally, intracisternally, intravaginally, intraperitoneally, topically (as by powders, ointments, or drops), bucally, or as an oral or nasal spray (page 8, lines 1-4).

Further, Wenzel teaches that the total daily dose of the compounds of formula I administered to a human in single or in divided doses can be in amounts, for example, from 0.05 to about 500 mg/kg body weight daily or more preferably from about 1 to about 150 mg/kg body weight for oral administration or 0.01 to about 10 mg/kg for parenteral administration daily (page 12, lines 37-40).

Katori teaches that COX-2 mediated diseases encompass acute exuditive inflammation, proliferative inflammation, animal arthritis, rheumatoid arthritis, angiogenesis, bone absorption, gastric ulcer, colon cancer, hyperalgesia, Alzheimer's disease, and certain states of the kidney, brain, and female reproductive organs (abstract).

Hofbauer teaches that NF-kβ mediated diseases include postmenopausal osteoporosis, rheumatoid arthritis, Paget's disease, periodontal disease, benign and malignant bone tumors, bone metastases, and hypercalcemia of malignancy (abstract).

Wenzel does not specifically teach a method for stimulating bone formation and/or inhibiting bone resorption.

It would have been obvious to one of ordinary skill in the art at the time of the invention to have employed the compounds of formula II, namely hesperidin, and derivatives thereof, to treat cyclooxygenase-2 (COX-2) and nuclear factor kappa B (NF-kβ) mediated diseases as taught by Wenzel that the stimulation of bone formation and inhibition of bone resorption would also be effected. As evidenced by Katori, COX-2

mediated diseases encompass bone absorption and as evidenced by Hofbauer, NF-kβ mediated diseases include postmenopausal osteoporosis, rheumatoid arthritis, Paget's disease, periodontal disease, benign and malignant bone tumors, bone metastases, and hypercalcemia of malignancy. Thus it would have been obvious that by administering hesperidin and derivatives thereof, one would be stimulating bone formation and/or inhibiting bone resorption which ultimately will have an effect on the remodeling of bone associated with such diseases (i.e., osteoporosis, Paget's disease, periodontal disease, benign and malignant bone tumors, bone metastases, etc.)

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wenzel et al. (EP 1127572A2) as evidenced by (Katori, et al., *Inflammatory Research*, 2000) and Hofbauer et al (*Journal of Molecular Medicine*, 2001) as applied to claims 2-8, 10-11, and 13-22 above in view of Barnes et al. (US Patent No. 5,506,211).

Wenzel is discussed above. Wenzel also teaches genistein (table 4).

Wenzel does not teach the nutritional composition of hesperidin or one of its derivatives in the form of animal feed in a wet, semi-wet, or dry form.

Barnes teaches genistein, which is used to provide a method of use in inhibiting osteoclast activity to reduce bone loss (ie, in patients with osteoporosis), may be present in a variety of foodstuffs, particularly soy products, and may be ingested by animals to provide them with an effective amount genistein (column 3, lines 5-10).

It would have been obvious to one of ordinary skill in the art at the time of the invention to have added hesperidin and genistein to food preparations for human consumption to treat bone related conditions as taught by Wenzel and also added it to food preparations designed for animals. The motivation, provided by Barnes, teaches that genistein may be incorporated in a variety of foodstuffs for animals to reduce bone loss. Since Wenzel teaches that hesperidin for the same purpose, it would also have been obvious to incorporate hesperidin into animal food preparations.

Conclusion

Claims 2-11 and 13-22 are not allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAHAR JAVANMARD whose telephone number is (571) 270-3280. The examiner can normally be reached on 8 AM-5 PM MON-FRI (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/S. J./

Examiner, Art Unit 1617

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617